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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/535,736	05/18/2005	Junichi Inagawa	B 520	9426

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EXAMINER	
HOBBS, LISA JOE	

ART UNIT	PAPER NUMBER
1657	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/535,736	INAGAWA ET AL.	
	Examiner	Art Unit	
	Lisa J. Hobbs	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 February 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15 and 18-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15 and 18-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Status

Claims 1-15, 18-21 are active in the case. Claims 16-17 have been cancelled by amendment. Claims 1-15 and 18-21 are under examination

.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-15 and 18-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wagner et al. (WO 2001/72458) in view of Bosman et al. (WO 1999/00670), Barner et al. (US 5986066), Badley et al. (US 6294391), Nelson et al. (US 5955729), and Nock et al. (US 2002/0049152 A1). Wagner et al. teach heterofunctional cross linking reagents, protein labeling reagents, protein conjugates and their compositions, support-bound cross linking groups, modified supports and protein arrays for site specific binding of proteins, they teach techniques for attaching a biomolecule (a protein) containing a tag by binding sites for the biomolecule tag and for covalently attaching a biomolecule to activated reactive groups (support-bound cross linking groups) to a solid support. Barner et al. teach cross-linking molecules, which molecules will biologically recognize target molecules, to a solid phase using carrier molecules. Bosman et al. teach methods of covalently immobilizing biomolecules by means of a His-tag and using a substrate that biologically recognizes the His tag. Badley et al. teach methods of detecting the presence of an analyte of interest in a sample, the method comprising the steps of: providing a binding partner reversibly immobilized on a solid support, said binding partner having binding specificity for the analyte; contacting the sample with the solid support; specifically displacing the binding partner from the solid support in response to the presence of the analyte of interest in the sample, said displacement causing a reduction in the mass of material immobilized on the solid support, thereby generating a detectable change in a mass-dependent property of the solid support; and detecting said change, while Nelson et al. teach detection of analytes using surface plasmon resonance.

Wagner et al. teach that it is known to attach a protein to a solid support by associating a protein containing a tag with a protein tag binder, see page 6, lines 3-10 (claims 1, 12, 18, and 20); they also disclose a method for covalently attaching a protein to the surface by linking groups (claim 2). Wagner et al. also teach the use of an amino group from the biomolecule and a carboxyl group of the sensor chip to create a covalent bond (claim 3). As well, Barner et al. explicitly state in columns 3 and 4 that reactive functional groups, such as COOH or NH_2 are well-known for use as covalent attachment points for immobilizing biomolecules (claims 2-3).

Additionally, Wagner et al. teach naturally binding molecules (claim 11), such as antigen/antibody recognition epitopes, as protein-tag binders. On page 13 they teach His tags (claims 9-10). However, they do not teach details of His tag antibody and antigen reactions. Bosman et al. teach detailed methods of using His tags and His tag antibodies, see entire document, including the complexing of glycoproteins to metal affinity resin on page 3 (claim 19).

At page 26, Wagner et al. teach the introduction of introduce histidine tags into the protein (claim 4) and then the binding of the protein to a sensor chip coated with nitrilotriacetic acid (NTA) through Ni2+ (claims 4-7). Wagner et al. do not teach the use of iminodiacetic acid (IDA), however it is taught by Bosman et al., page 3, that IDA/Ni2+ can be used as an alternative to NTA in His tag immobilization (claim 8).

Wagner et al. do not specifically teach low molecular weight compound binding (claims 13 and 15), however they, Barner et al., and Bosman et al., do describe multiple binding substituents, including a statement by Bosman et al. that the invention is "to simultaneously provide a universal detection method for biomolecules that contain a His tag", page 5, and

Wagner et al. teach protein-protein, protein-nucleic acid, protein-drug, and protein-ligand interactions, see page 2, which encompasses a large range of molecular weights.

The use of surface plasmon resonance to measure and detect biomolecules and analytes of interest (claim 14) is known in the art, as described by Nelson et al., see entire document, while Badley et al. specifically teach methods of detecting the presence of an analyte of interest in a sample, the method comprising the steps of: providing a binding partner reversibly immobilized on a solid support, said binding partner having binding specificity for the analyte; contacting the sample with the solid support; specifically displacing the binding partner from the solid support in response to the presence of the analyte of interest in the sample, said displacement causing a reduction in the mass of material immobilized on the solid support, thereby generating a detectable change in a mass-dependent property of the solid support; and detecting said change, paragraph 23, using "a number of mass-dependent properties which can be detected, for example, by acoustic wave or evanescent wave type sensors, or by surface plasmon resonance (SPR) detectors, all of which are known in the art".

Nock et al. teach "methods for immobilizing polypeptides, for forming arrays of polypeptides arranged on a support, and arrays produced using the methods of the invention. The immobilized polypeptides of the invention are generally in the same orientation, can be full-length and biologically active, and can be readily screened for a desired activity" (abstract). They specifically teach that "[t]he methods of the invention can also be used with trifunctional linkers". "These linkers are useful for the site-specific introduction of a label to a polypeptide, in addition to the site-specific immobilization of a polypeptide to a solid support. These trifunctional crosslinking groups have, in some embodiments, [a] formula wherein W is a

trivalent core component; L.sup.1, L.sup.2 and L.sup.3 are independently linking groups; X is a non -covalent polypeptide tag binder; Y is a photoactivatable covalent linking group; and Z is a protected or unprotected covalent crosslinking group. In this particular example, a trifunctional linking group is depicted having three functional groups (X, Y and Z) attached via linkers (L.sup.1, L.sup.2 and L.sup.3) to a central core (W). The first functional group is one which provides a non -covalent association with a targeted polypeptide or a polypeptide of interest. For example, the trifunctional linking group can form a non -covalent association complex with a polypeptide having a suitable tag (e.g., a his-tag). The second functional group can then establish a covalent linkage to the polypeptide at a site which is proximate to the initial non -covalent association site. One of skill in the art will appreciate that although the polypeptide is shown as a relatively small circle (relative to the size of the trifunctional crosslinking group), in fact the polypeptide in most embodiments is quite large relative to the crosslinking group. Nevertheless, the site for covalent attachment of functional group Y will depend on the lengths and flexibility of the linking groups L.sup.1 and L.sup.2. Typically, the site for covalent attachment of Y to the polypeptide will be within about 50 angstroms of the site of non -covalent association. Release of the non -covalent functional group (X) from the polypeptide provides a polypeptide having a covalently bound trifunctional crosslinking group. In subsequent steps, functional group Z of the polypeptide-crosslinking group composition can be used, for example, to attach a suitable label to the polypeptide, or to immobilize the polypeptide on a suitable support' [0099-0100].

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Wagner et al. with Barner et al., Bosman, et al., Badley et al., Nelson et al., and Nock et al. in order to achieve the invention as claimed in the claims under

examination. As demonstrated above, methods for the immobilization of biomolecules involving covalent binding of substituents by chemical groups or by antibody/antigen binding, assisted by other chemicals, using components naturally present or added to the molecules as needed, were known in the art and the claims, as presented, are rendered obvious.

Response to Arguments

Applicant's arguments filed 27 February 2009 have been fully considered but they are not persuasive. Applicant argues that the references cited neither teach nor suggest a method of immobilizing a biomolecule to a substrate having both tag binding sites and activated reactive groups. However, Bosman et al. discuss the use of His tags in immobilization of biomolecules and the specifics of using tags with and without additional covalent binding to the support. They discuss a method "wherein the presence of His-tags is exploited for covalent immobilisation of a biomolecule that contains said His-tag, and wherein the amino acid residues that comprise said His-tag are directly involved in the covalent bond" (page 5). As well, they describe methods to increase the probability of a reaction with the his residues of the His-tag of the biomolecule, while increasing the reaction of the membrane or carrier to which said biomolecule has to be immomobilised covalently (page 9). Finally, on page 12, they discuss that biomolecules that use His-tags as crosslinking elements as well as the biomolecule being involved in a covalent immobilization forming an aggregate. On page 13, they specifically describe the inclusion of methods for covalent linkage between two biomolecules, of which at least one, or sometimes both, contains a His-tag.

Applicants particularly argue that Bosman et al. do not specifically teach that the second form of binding occurs specifically between non-tag elements of the construct. This argument

has been considered but is not persuasive. Claim 1 recites that the biomolecules of interest have at least one tag which will bind to the immobilization substrate and also have "reactive groups which are **capable of** forming covalent bonds with the non-tag part of the biomolecule" (emphasis added) but does not specify that the second bond must be to the non-tag part of the biomolecule.

With the current amendments applicants have rendered moot the argument that the dependent claims do not clearly state that while one interaction is between the tag on the biomolecule and the tag-binding portion of the substrate, the second bond is not clearly recited as being not related to the tag, i.e., a covalent bond between reactive groups and non-tag portions of the biomolecule. However, as has been discussed in prior actions, at the time of filing, this type of multiple binding was known in the prior art. Nock et al. is added to make clear that biomolecules with multiple, concurrent forms of binding to supports and other compounds of interest was known in the art, including binding of tags with concomitant covalent binding, as well as other bonds forming the ability to add additional partners.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa J. Hobbs whose telephone number is 571-272-3373. The examiner can normally be reached on Hotelling - Generally, 9-6 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Lisa J. Hobbs/
Primary Examiner
Art Unit 1657

ljh